Reviewer's report

Title: Analysis of EIF4G1 gene with Parkinson's disease in ethnic Chinese population

Version: 2 Date: 10 December 2012

Reviewer: Carles Vilarino-Guell

Reviewer's report:

I am very disappointed to see that the editor suggested adding GIGYF2 to the list of genes implicated in PD. Although this gene was nominated as a PD gene in 2008, dozens of publications have invalidated this claim over the last few years. As examples, please see http://www.ncbi.nlm.nih.gov/pubmed/19250854 or http://www.ncbi.nlm.nih.gov/pubmed/19279319 or http://www.ncbi.nlm.nih.gov/pubmed/19348706 or http://www.ncbi.nlm.nih.gov/pubmed/18923002 or http://www.ncbi.nlm.nih.gov/pubmed/19117363 or http://www.ncbi.nlm.nih.gov/pubmed/19133664 or http://www.ncbi.nlm.nih.gov/pubmed/19321232 amongst many others. Please do NOT add GYGIF2 to the list of genes implicated in PD in your introduction. This was a really poor comment by the editor, and I hope in the future she considers up to date literature before making this kind of comments.

Similarly, Omi/Htra2 is conclusively not a gene implicated in PD biology. Although several inconclusive but suggestive papers have been published since the initial report, and reviews still continue to mention them, over the last few years an enormous amount of data has been generated proving that Omi/Htra2 is not implicated in PD, and it is time to stop promoting the erroneous data. Even the author of the original identification of Omi in PD is now confirming that this gene is not implicated in disease (http://www.ncbi.nlm.nih.gov/pubmed/20036034). Moreover, the originally described as pathogenic mutation (p.G399S) has been identified in cases and controls at similar frequencies (1%) (http://www.ncbi.nlm.nih.gov/pubmed/18790661). There are many other report like those, and the conclusion is that Omi/Htra2 is not a PD gene and should never again be considered or mentioned as a PD gene. The mention of GYGIF2 and Omi are the kind of quotes that keep misleading the field and wasting people’s time doing functional research which is irrelevant to the disease.

Regarding the manuscript, the authors have addressed most of the concerns and it is much improved. In reference to the analysis with one or two degrees of freedom, the authors should understand that the three genotypes are not independent values, as they are dependent on allele frequencies; in a way the first genotype is p-squared, the second is 2pq and the third is q-squared; therefore only two variables p and q are present, and hence only one degree of freedom is the appropriate analysis. Please correct the values on the table to
represent a one degree of freedom analysis.

Minor comments

In several instances, the authors refer to previously reported pathogenic mutations as “mutations”, this is not very clear and doesn’t read right. These should be corrected probably to “previously reported pathogenic mutations” or “reported mutations” or something similar, and these are found in page 2 line 11; page 5 line 2 from the bottom and page 6 line 5 from the bottom.

In page 4 the authors write “The translation initiation complex is a large family, including eukaryotic translation initiation factor 4E, eukaryotic translation initiation factor 3e (eIF3e) and so on.” I believe this sentence would read better as “The translation initiation complex is a large family, including eukaryotic translation initiation factor 4E and eukaryotic translation initiation factor 3e (eIF3e)”

The authors state in two places that “the eight intronic variants are in introns” this is rhetoric and unnecessary, and should be removed. Also in page 6 line 3; it would be better to describe the “two exonic variants” as “two nonsynonymous variants”.

In several instances the authors report exon numbers without a space from the exon (ie exon27); a space should be added between the exon and the number. A few similar errors with spacing can be found throughout the manuscript.

The new title is not grammatically correct… it read as if EIF4G1 has Parkinson’s disease… I would suggest “Analysis of EIF4G1 in ethnic Chinese Parkinson’s disease patients” or “Analysis of EIF4G1 in ethnic Chinese”. Although the grammar has been significantly improved, a final double checked would be welcomed.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests